may contribute to different subsets of patients with NDG. Future clinical studies need to examine the utility of looking for these co-morbidities in patients presenting with idiopathic gastroparesis. Equally importantly, DG appears to be part of the spectrum of microvascular complications, and if so, may be preventable with better glycemic control.

Table 1. Autoimmune and Female specific Comorbidities in Nondiabetic vs. Diabetic Gastroparesis

Autoimmune Comorbidities			Disorders of Female Organs		
Co-morbidity	RR	95% CI	Co-morbidity	RR	95% CI
Multiple Sclerosis	4.8	4.4-5.3	Ovarian Cysts	3.2	2.9-3.6
Inflammatory Bowel Disease	4.8	4.4-5.2	Endometriosis	3.2	2.7-3.8
Connective Tissue Disorders	4.2	4.0-4.5	Menopausal disorders	2.0	1.6-2.5
Rheumatoid Arthritis	2.0	1.9-2.2	Menstrual disorders	1.6	1.4-1.8

Table 2. Cardiovascular Co-morbidity in Diabetics with and without Gastroparesis

Microvascular Co-morbidity			Macrovascular Co-morbidity		
Co-morbidity	RR	95% CI	Co-morbidity	RR	95% CI
Retinopathy	4.41	4.36-4.46	Coronary artery disease	0.68	0.67-0.68
Nephritis	3.31	3.28-3.36	Cardiac arrest	0.43	0.40-0.47
Noncongenital Nervous system disorders	2.25	2.23-2.26	Acute CVA	0.40	0.38-0.41
Chronic renal failure	2.13	2.11-2.15	Acute MI	0.37	0.36-0.38

M1208

Symptom-Based Subgroups in Functional Dyspepsia: A Cluster Analysis Approach

Lukas Van Oudenhove, Lieselot Holvoet, Rita Vos, Raf Bisschops, Joris Arts, Philip Caenepeel, Dominiek De Wulf, Koen Demyttenaere, Jan F. Tack

Introduction: The Rome III consensus proposed to subdivide functional dyspepsia (FD) into epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS), based on the symptom pattern (Tack et al, Gastroenterology 2006). The same consensus proposed to consider separate diagnostic categories for nausea/vomiting and for belching disorders. ***Aim:*** To empirically investigate the validity of this symptom-based subgrouping. ***Methods:*** In 705 consecutive tertiary care patients, clinically diagnosed with FD according to Rome II criteria, the severity of 8 FD symptoms (pain, fullness, bloating, early satiation, nausea, vomiting, belching & epigastric burning) was scored on a Likert scale [range: 0-3 (absent, mild, moderate, severe)]. First, hierarchical cluster analysis with Ward's clustering method was used to determine the most appropriate number of clusters for subsequent non-hierarchical cluster analysis. Second, non-hierarchical cluster analysis with full seed replacement was performed to determine the optimal cluster solution. ***Results:*** The median (IQR) score was 2 (0-2) for pain & early satiation, 2 (1-3) for fullness, 2 (1-2) for bloating, 1 (0-2) for nausea, belching & epigastric burning and 0 (0-1) for vomiting. Hierarchical cluster analysis suggested a 4 cluster solution, based on the R^2 method. Non-hierarchical cluster analysis with 4 clusters on all 8 variables showed very low R^2 values for the variable belching, indicating that it may no be sufficiently appropriate for forming clusters. Therefore, this variable was removed from the final analysis. Non-hierarchical cluster analysis with 4 clusters on the 7 remaining variables resulted in an overall R^2 of 0.37, indicating considerable overlap between the clusters. Vomiting, pain and early satiation were found to be the most important variables separating the clusters, with R^2 values of 0.67, 0.54 and 0.52, respectively. The first cluster was characterized by high early satiety, fullness & bloating and moderate pain ('postprandial distress cluster'). The second cluster was characterized by high vomiting, nausea and fullness ('nausea-vomiting cluster'). The third cluster was characterized by high pain ('epigastric pain cluster'). The fourth cluster was characterized by low scores on all symptoms ('limited severity cluster'). ***Conclusion:*** The symptom-based subgroups from the Rome III criteria are supported by the present data which confirmed the existence of EPS and PDS subgroups and a nausea/vomiting cluster. On the other hand, another 'low severity" subgroup was also identiefied and overlap between subgroups is considerable.

M1209

Reduced Stool Frequency Does Not Predict Colonic and Whole Gut Transit in Constipated Patients

Richard J. Saad, William D. Chey, Satish S. Rao, William L. Hasler, Leonard A. Katz, Kenneth L. Koch, Braden Kuo, Jeffrey M. Lackner, Henry P. Parkman, Richard McCallum, Carrie Miller, Irene Sarosiek, Jack Semler, Michael D. Sitrin, Gregory E. Wilding

Background: Normal stool frequency is traditionally defined as >3 bowel movements (BMs) per week and fewer than 3 BMs per day. We have previously reported that overall stool frequency correlates poorly with whole gut transit. It has been suggested that abnormally reduced stool frequency (<3 BM/wk) may provide a better surrogate means of identifying patients with slow transit. Aim: To assess the correlation between abnormally reduced stool frequency in constipated adults with whole gut and colonic transit time. Methods: 78 adults with chronic constipation (CC) from 9 U.S. sites recorded stool frequency during simultaneous assessment of whole gut and colonic transit with Smartpill® (SP) and a radio-opaque marker test (ROM) using the Hinton method. In a post-hoc analysis, participants were divided into 4 groups based upon their weekly stool frequency (<6, <5, <4, <3 BM/wk). Stool frequency was correlated with transit times using Spearman's rank correlation. Results: The mean daily bowel movement frequency for CC was 0.9. The mean whole gut transit was 72.2 hours and mean colonic transit was 62 hours as measured by SP in CC. The mean 5-day ROM count was 7.0 in CC. Overall, there was a poor correlation between stool frequency and transit (SP whole gut transit: r = -0.10 (p =0.47, n = 62), SP colonic transit: r = -0.10 (p = 0.45, n = 62) ROM colonic transit: r = 0.09 (p = 0.48, n = 60). Correlation data stratified by weekly stool frequency are presented in the table. Conclusions: In constipated adults, stool frequency correlates poorly with whole gut and colonic transit time. This statement is true even in those with abnormally reduced stool frequency. As such, abnormally reduced stool frequency should not be used to identify patients with slow transit in the physician's office or clinical trials. When a precise estimate of transit is necessary, formal evaluation with an objective testing modality should be pursued.

Spearman correlation of stool frequency with transit based on weekly BM frequency

	Whole Gut Transit by SmartPill®	Colonic Transit by SmartPill®	Day 5 Sitzmark® Count
Less than 3 bowel movements a week	0.64 n = 16	0.63 n = 16	0.54 n = 17
Less than 4 bowel movements a week	-0.30 n = 24	-0.26 n = 24	0.004 n = 26
Less than 5 bowel movements a week	-0.23 n = 40	-0.26 n = 40	0.13 n = 41
Less than 6 bowel movements a week	-0.12 n = 47	-0.19 n = 47	-0.003 n = 47

M1210

Subgroups in Functional Dyspepsia: A Cluster Analysis Approach Based On the Interaction of Symptom Severity, Gastric Sensitivity and Psychosocial Factors

Lukas Van Oudenhove, Lieselot Holvoet, Rita Vos, Raf Bisschops, Joris Arts, Philip Caenepeel, Dominiek De Wulf, Koen Demyttenaere, Jan F. Tack

Introduction Functional dyspepsia (FD) is a heterogeneous biopsychosocial disorder. The Rome III consensus proposed a subdivision based on symptom pattern only into epigastric pain syndrome and postprandial distress syndrome (Tack et al 2006). It remains unclear whether considering psychosocial factors and visceral sensitivity would lead to a different subdivision. ***Aim*** To investigate the presence of subgroups within FD, based on symptom severity, gastric sensitivity and psychosocial factors. ***Methods*** In 201 consecutive tertiary care patients, clinically diagnosed with FD (Rome II), gastric sensitivity was measured using barostat. Dyspepsia symptom severity (DSS), trait anxiety, present anxiety, depression and somatization were quantified using validated self-report questionnaires. First, hierarchical cluster analysis with Ward's clustering method was used to determine the most appropriate number of clusters for subsequent non-hierarchical cluster analysis. Second, non-hierarchical cluster analysis with full seed replacement was performed to determine the optimal cluster solution. ***Results*** Hierarchical cluster analysis suggested a 4 cluster solution, based on the R^2 method. Non-hierarchical cluster analysis with 4 clusters on all 6 variables resulted in an overall R^2 of 0.45, indicating considerable overlap between the clusters. All variables had sufficiently high R^2 values, indicating that all contributed significantly to cluster formation. Present anxiety, depression and somatization were found to be the most important variables separating the clusters, with R^2 values of 0.58, 0.56 and 0.45, respectively. The first cluster was characterized by low discomfort threshold as well as high DSS and somatization ('hypersensitivity-somatization cluster'). The second cluster was characterized by low discomfort threshold, moderate to high DSS & trait anxiety, high present anxiety & depression and moderate to high somatization ('hypersensitivity-psychiatric-somatization cluster'). The third cluster was characterized by high discomfort threshold, low DSS, high trait anxiety and moderate present anxiety, depression & somatization ('normosensitivity-trait anxiety cluster'). The fourth cluster was characterized by moderate to high discomfort threshold and low scores on all other variables ('limited severity cluster'). ***Conclusion*** Using a cluster analysis approach taking into account symptom pattern, psychosocial factors and visceral sensitivity, we identified four subgroups within FD. However, there was still considerable overlap between clusters. Present anxiety, depression and, to a lesser extent, somatization are the most important factors seperating subgroups.

M1211

Is There Any Association Between Disturbed Gastrointestinal Visceromotor and Sensory Function and Impaired Quality of Life in Functional Dyspepsia? A Population-Based Study.

Sebastian Haag, Wolfgang Senf, Sefik Tagay, Guido Gerken, Nicholas J. Talley, Gerald Holtmann

Background: Functional dyspepsia (FD) is now categorized into the epigastric pain syndrome (EPS) and the postprandial distress syndrome (PDS). However, EPS and PDS have not been studied with regard to the role of disturbed gastric emptying and sensory functions for the reduction of HRQOL. **Methods:** 300 refractory FD patients and 450 healthy blood donors (BD) were studied. BD were stratified in subjects with (BD+) and without (BD-) concomitant FD symptoms. Gastric motor (C13-octanoic breath test) and sensory function (liquid load test), generic and disease-specific HRQOL (SF-36, physical [PCS] and mental component score [MCS], Nepean Dyspepsia Index) and affective disorders (Hospital Anxiety and Depression Scale) were assessed. Twenty randomly selected asymptomatic BD-, 50 (36 PDS, 72%) symptomatic BD+, and 110 FD (95 PDS, 86.4%) patients had additional function testing. **Results:** HRQOL was significantly reduced in FD patients (PCS = 40.7±8.8, MCS = 39.7±11.3, both p<0.0001) compared to BD+ (PCS = 52.0±7.6, MCS = 49.0±9.4) and BD- (PCS = 56.0±4.3, MCS = 52.8±7.2). GET (t ½, min) was significantly (both p<0.0001) longer in FD patients (143.0±7.3) compared to BD+ (101.1±6.3) and BD- (73.8±7.6). While FD patients scored significantly higher for "pain" (p<0.0001) and "nausea" (p=0.023) there was no difference for "fullness" compared to BD. Impairment of GET was not associated with HRQOL. In FD patients, diminished sensory function (fullness, nausea) was associated with MCS. There was no difference between FD patient categorized as having EDS or PDS. **Conclusion:** In EPS and PDS, delayed gastric empting and altered sensory function are

disease markers but not directly linked to the severity of HRQOL impairment or clinical presentation of FD.

M1212

Do IBS Symptoms Vary Between Men and Women? a Meta-Analysis
Mopelola A. Adeyemo, Brennan M. Spiegel, Lin Chang

Introduction: IBS is a female predominant disorder marked by abdominal pain and altered bowel habits. Sex differences in IBS have been reported with regard to prevalence, clinical symptoms, response to treatment, and physiology. There is also evidence for increased symptoms and enhanced visceral perception at time of menses, suggesting that female sex hormones may be a contributing factor. However, data regarding sex differences are limited and conflicting. We performed a meta-analysis to: 1) compare the prevalence of IBS symptoms between sexes, 2) examine the effect of menstrual cycle on IBS symptoms, and 3) examine the effect of menopausal status on IBS symptoms. **Methods:** We performed a systematic review of MEDLINE to search for studies comparing IBS symptoms between sexes, menstrual cycle phases, and menopausal states in IBS and/or healthy individuals. We performed meta-analysis to compare the relative risk (RR) of IBS symptoms between sexes. **Results:** There were 13 studies reporting sex differences in IBS symptoms. In both the general population and IBS patients, the RR for each cardinal symptom was higher in women than men, although the difference for some symptoms was insignificant (**Table**). Eleven studies measured IBS symptoms by menstrual cycle, and 40-60% of patients in these studies reported increased prevalence and severity of bloating, gas, loose stools, and pain during menses *vs.* other times of the cycle. Of the 3 studies evaluating the effect of menopause on GI symptoms, only nausea was more prevalent in pre- *vs.* post-menopausal women with IBS. In healthy women, gas and flatulence were more prevalent in the post- *vs.* pre-menopausal women. **Conclusion:** Women are more likely to report IBS symptoms than men, particularly those associated with constipation. This may help explain the female predominance in IBS-C and chronic constipation, in particular. Female sex hormones may influence IBS symptoms, but larger studies with more accurate assessment of menstrual cycle phases are needed.

Table.

Symptom	# studies (Overall)	RR favoring women (95% CI)	# studies (IBS Only)	RR favoring women (95% CI)
Distension	6	1.32 (1.14,1.51)	4	1.39 (1.20,1.61)
Bloating	8	1.16 (1.04,1.29)	4	1.22 (1.05,1.42)
Incomplete evacuation	10	1.11 (1.02,1.20)	6	1.24 (1.03,1.50)
Infrequent stools	4	1.11 (1.03,1.19)	1	NA
Abdominal pain	5	1.11 (1.01,1.23)	1	NA
Lumpy/hard stools	7	1.10 (0.98,1.23)	4	1.24 (1.09,1.41)
Straining	8	1.09 (1.01,1.18)	4	1.02 (0.91,1.14)
Urgency	7	1.06 (0.98,1.16)	4	1.11 (1.02,1.21)

NA=Not applicable (insufficient studies). Supported by NIH grants P50 DK64539-06S1, DK64539 and R24 AT002681.

M1213

IBS Patients Show Parasympathetic Dominance in Heart Rate Variability Compared to Healthy Controls
Chloé E. Hill, Olafur S. Palsson, Motoyori Kanazawa, Marsha J. Turner, William E. Whitehead

Background and Aims: Previous studies of heart rate variability (HRV) found differences between patients with irritable bowel syndrome (IBS) and healthy controls suggesting parasympathetic dominance in IBS. Altered autonomic activation may explain differences in gastrointestinal motility or pain sensitivity. Our aims were (1) to replicate findings of greater parasympathetic drive in IBS, and (2) to assess the correlation of HRV to pain threshold and motility measured by the barostat technique. **Methods:** Autonomic measurements were collected from 129 IBS patients meeting Rome III criteria (30 IBS-C, 43 IBS-D, 45 IBS-A, 11 IBS-U) and 25 healthy controls during rest, pain testing, sustained rectal distention, and following a high-fat meal. HRV was calculated by frequency domain analysis of 15-minute EKG segments obtained during each condition. Low frequency (LF) and high frequency (HF) bands were analyzed to assess sympathetic and parasympathetic activity, respectively, and the LF/HF ratio was calculated. **Results:** *Between-subject comparisons* — (1) There were no differences in HRV between IBS patients and controls at rest, but IBS patients showed more HF power (parasympathetic activation) and less LF power (sympathetic activation) following the meal (both $p<0.01$). The LF/HF ratio was also less in IBS during sustained intraluminal distention compared to controls ($p<0.01$). (2) There were no differences between IBS-C and IBS-D for any condition. *Within-subject comparisons* - (3) Each stimulation condition- visceral pain, sustained distention, and eating- significantly increased LF power for both IBS patients and controls, but there were no differences between groups in reactivity to these stimuli. (4) IBS-C patients showed an increase in LF power in response to painful as well as non-painful distention that was not seen in IBS-D ($p<0.01$). *Relation of HRV to pain sensitivity and motility* - (5) Pain threshold correlated $r= -0.23$ ($p<0.03$) with LF power during sustained distention in IBS patients. (6) Postprandial motility correlated $r= 0.18$ ($p<0.05$) with postprandial LF power in IBS patients). (7) Postprandial change in barostat volume correlated $r=0.49$ ($p<0.02$) to postprandial LF/HF ratio in controls. **Conclusions:** These data confirm that IBS patients show greater parasympathetic activation than controls in response to provocative stimuli, and extend these observations by showing greater sympathetic activation in IBS-C compared to IBS-D. Correlations of HRV with pain threshold, phasic motility, and smooth muscle tone are statistically significant but weak. [Supported by R01 DK31369, R24 DK067674, RR00046, and U54RR024383]

M1214

Stability of Gastrointestinal Symptom Severity After One Year in IBS Patients
Per Jerndal, Gisela Ringstrom, Pia Agerforz, Magnus Simren

Background: Gastrointestinal (GI) symptom severity is known to fluctuate periodically in IBS patients. Whether symptom severity changes during a longer period of time is largely unknown. Aim: To assess change in GI symptoms in IBS patients and factors related to change. Method: We included 275 patients fulfilling the Rome II criteria for IBS, who were evaluated at baseline with five different questionnaires: A combination of the Gastrointestinal Symptom Rating Scale (GSRS) and GSRS-IBS, the Visceral Sensitivity Index (VSI), the Hospital Anxiety and Depression Scale (HAD), the Short Form-36 (SF-36), and Sense of Coherence. One year later patients were asked to complete the same questionnaires. One hundred eighty patients (122 females; mean age 42 years) had valid GSRS questionnaires at both baseline and at one year follow up and formed the basis for the analyses (68%). Results: In our cohort of patients 80% had had their IBS symptoms for more than five years, and 74 had IBS-D (diarrhea) (41%), 36 IBS-C (constipation) (20%) and 70 IBS-A (alternating type) (39%). On average the total GI symptom severity was mild to moderate at baseline, with bloating, flatulence and abdominal distension being ranked as the most severe symptoms. A change in GSRS total score from baseline to one year follow up of more than 25% was defined as clinically significant symptom improvement / deterioration. With this definition, 69% of the patients had unchanged GI symptom severity, whereas 19% were improved and 12% deteriorated. When comparing baseline data between the three groups of patients (unchanged/improved/deteriorated) only GI symptom severity was associated with the outcome. Patients with a higher symptom score (i.e. more severe symptoms) on GSRS total score and the dimensions abdominal pain, indigestion, diarrhea and satiety at baseline were significantly more likely to be in the improved group whereas patients with a lower score (i.e. less severe symptoms) were significantly more likely to be in the group of patients whose GI symptoms had deteriorated ($p<0.001$). Anxiety, depression, GI-specific anxiety, coping or quality of life did not differ between the three groups at baseline. No association between change in GI symptom severity at one year and duration of IBS symptoms, IBS subgroup, gender or sexual abuse could be found. Conclusion: When evaluated at one year, the majority of patients with IBS have unchanged GI symptom severity. Except for GI symptom severity at baseline, we could not find any factors predicting the outcome. Further studies are needed to better understand the long-term natural history of IBS.

M1215

Unexplained Gastrointestinal Dysmotility and Joint Hypermobility: Is Connective Tissue the Missing Link?
Adam D. Farmer, Natalia Zarate, S Mark Scott, Sahar Mohammed, Charles H. Knowles, Rodney Grahame, Qasim Aziz

INTRODUCTION: Gastrointestinal (GI) symptoms of unexplained aetiology are common in the general population and patients are often classified as having functional gastrointestinal disorders (FGIDs) or idiopathic dysmotility. Generalised joint hypermobility (JHM) is an equally common phenomenon and when patients present with musculoskeletal symptoms a diagnosis of benign joint hypermobility syndrome (BJHS) may be made based on validated criteria [1]. BJHS is a non-inflammatory and non-progressive genetically determined disorder that represents a symptomatic expression of JHM. The epidemiology and co-morbidity of BJHS and FGIDs bear striking resemblances. In fact, a pathophysiological link through abnormalities of connective tissue is scientifically plausible. AIMS & METHODS: We aimed to prospectively evaluate the incidence of JHM and BJHS in a cohort of patients' referred to a tertiary referral Neurogastroenterology clinic. A 5-point well validated questionnaire was used to detect JHM [2]. A rheumatologist who specialises in JHM related disorders performed further evaluation of a proportion of these patients. RESULTS: 72/115 (62.6%) patients (58 females, median age 38 years, age range 17-78 years) had GI symptoms without a known underlying structural, metabolic or autoimmune disorder or in the absence of a unifying diagnosis at the time of referral and had been labelled in secondary care as having a FGID. 42/72 (58.3%) (34 females, median age 32 years, age range 17-57 years) had evidence of generalised JHM. 18/42 (42.8%) patients were randomly selected and referred to the rheumatologist who confirmed JHM in 16/18 (88.8%), with 11/18 (61.1%) receiving a formal diagnosis of BJHS. Patients with co-existent BJHS and previously unexplained GI symptoms experienced symptoms suggestive of a sluggish gut biomechanics: bloating (72.2%), reflux (56%), constipation (39%) and nausea (33.3%). 9/11 (81.8%) patients presenting with upper GI symptoms had delayed gastric emptying. 10/12 (83.3%) patients with lower GI symptoms had demonstrated abnormal small bowel manometry and/or delayed colonic transit. CONCLUSIONS: There is a high incidence of JHM in patients referred to tertiary care with unexplained GI symptoms and in a proportion of these a diagnosis of BJHS is made. In a large proportion, symptoms and functional tests suggest GI dysmotility, which could be secondary to lax gut connective tissue. The possibility that patients with unexplained GI symptoms and JHM may share a common pathophysiological disorder of connective tissue laxity warrants further investigation. REFERENCES: 1.Grahame R et al, J Rheumatol 2000. Hakim AJ et al, Int J Clin Pract 2003.

M1216

Gastroparesis Cardinal Symptom Index (GCSI): Use of a Daily Diary Versus Two Week Recall
Henry P. Parkman, Michael Camilleri, Braden Kuo, Nancy J. Norton, Susmita Paladugu, Lindsey Murray, Andrew Palsgrove, Dennis A. Revicki

The Gastroparesis Cardinal Symptom Index (GCSI) is used as a patient reported outcome for gastroparesis (Revicki 2003). Nine symptoms are assessed, for which the patient grades the severity of their symptoms from 0 (none) to 5 (very severe) over the prior 2 weeks. The